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L21	asthma\$3.ti,ab,clm. and (antifungal or anti-fungal or anti-mycotic or antimycotic)	175	L21
L20	L19 and (nasal or aerosol or spray or mucosal or mucoadministration)	144	L20
L19	asthma\$3.ti,ab,clm. and (antifungal or anti-fungal or anti-mycotic or antimycotic or fungistat\$2)	189	L19
L18	L17 and (nasal or aerosol or spray or mucosal or mucoadministration)	80	L18
L17	asthma\$3 same (antifungal or anti-fungal or anti-mycotic or antimycotic or fungistat\$2)	110	L17
L16	L15 and (nasal or aerosol or spray or mucosal or mucoadministration)	23	L16
L15	l2 and (amphotericin or ketoconazole or itraconazole or saperconazole or voriconazole)	23	L15
L14	l13 and (amphotericin or ketoconazole or itraconazole or saperconazole or voriconazole)	172	L14
L13	L12 and (antifungal or anti-fungal or anti-mycotic or antimycotic or fungistat\$2)	559	L13
L12	L11 and (nasal or aerosol or spray or mucosal or mucoadministration)	4546	L12
L11	l1 and (nystatin or amphotericin or macrolide or sterol inhibitor or \$5conazole or flucytosine or griseofulvin or \$7azole or ciclopirox olamine or haloprogin or tolnaftate or naftifine or terbinafine or morpholine or natamycin or butenafine or undecylenic or propionic acid or caprylic acid or whitefield\$2 ointment)	6761	L11
L10	L9 not l5	49	L10
L9	L8 and (nasal or aerosol or spray or mucosal or mucoadministration)	69	L9
L8	l3 and (nystatin or amphotericin or macrolide or sterol inhibitor or \$5conazole or flucytosine or griseofulvin or \$7azole or ciclopirox olamine or haloprogin or tolnaftate or naftifine or terbinafine or morpholine or natamycin or butenafine or undecylenic or propionic acid or caprylic acid or whitefield\$2 ointment)	77	L8
L7	L6 and (nasal or aerosol or spray or mucosal or mucoadministration)	26	L7
L6	L3 and (antifungal or anti-fungal or anti-mycotic or antimycotic or fungistat\$2)	26	L6
L5	L4 and (nasal or aerosol or spray or mucosal or mucoadministration)	45	L5
L4	L3 and (fungal or fungus or antifungal or anti-fungal or mycotic or mycosis or anti-mycotic or antimycotic or fungistat\$2)	58	L4
L3	L2 and l1	235	L3
L2	rhinosinusitis or ((rhinitis or catarrh\$2) and sinusitis) or sinisorhinitis or (inflammation near ((nose or nasal) and paranasal and muco\$3))	398	L2

L1     asthma\$3

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1: *Allergy* 1996 Dec;51(12):887-92

Related Articles, Books

Allergenicity of acid protease secreted by *Candida albicans*.Akiyama K, Shida T, Yasueda H, Mita H, Yanagihara Y, Hasegawa M,  
Maeda Y, Yamamoto T, Takesako K, Yamaguchi H

National Sagami Hospital, Kanagawa, Teikyo University, Tokyo, Japan.

We have previously reported the cases of *Candida albicans* (C. alb) acid protease (CAAP)-induced atopic asthma. In this study, the allergenicity of the released enzyme CAAP was examined among asthmatic patients with positive immediate skin response to crude C. alb antigen. Among 49 patients with positive skin response to crude C. alb, anti-crude C. alb IgE antibodies were detected in 40 and anti-CAAP IgE antibodies were detected in 18. Moreover, anticrude C. alb IgE antibodies were detected in all of the patients in whom anti-CAAP IgE antibodies were detected. No correlations between IgG antibodies to both antigens or between IgE and IgG antibodies to CAAP were observed. CAAP induced significant T-cell proliferation in 20/28 patients showing positive T-cell proliferation response to crude C. alb antigen. Most of the patients showing positive conjunctival response to crude C. alb antigen also showed positive response to CAAP. Most of the patients showing high levels of serum IgE antibody and positive histamine-release response of peripheral blood leukocytes to CAAP showed positive conjunctival response. The results indicate that CAAP is an important allergen in C. alb-related mucosal allergy.

PMID: 9020416, UI: 97172332

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1: *J Med Vet Mycol* 1995 Mar-Apr;33(2):127-30

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Fungal cultures on cyanoacrylate skin surface strippings as a dose-finding method for topical antifungals. A placebo-controlled study with 0.25% and 0.50% itraconazole cream.

Arrese JE, Schrooten P, de Doncker P, de Smett H, Cauwenbergh G, Pierard-Franchimont C, Pierard GE

Department of Dermatopathology, CHU Sart Tilmon, Liege, Belgium.

The antimycotic activities of 0.25% and 0.50% itraconazole cream were compared in the stratum corneum after once-daily applications for 1 week. Two groups of 12 healthy volunteers applied either itraconazole or placebo on the inner side of each forearm, in a double-blind design. Cyanoacrylate skin surface strippings (CSSS) were taken on days 8, 11 and 21. Conidia or yeasts of selected fungi (*Trichophyton rubrum*, *Trichophyton metagrophytes*, *Microsporum canis* and *Candida albicans*) were deposited on CSSS. Fungal growth on CSSS was assessed in time by computerized image analysis to derive the inhibitory effect of the previously applied antifungal preparations. Comparable antimycotic activity was found against dermatophytes for both concentrations. Itraconazole 0.50% appeared to be more active than 0.25% against *C. albicans*. The 0.50% concentration yielded prominent fungitoxic effect after 1 week of treatment, and showed a lingering effect in the stratum corneum for at least 3 days. This method could be useful in a pre-clinical setting and serve as a predictive tool for further clinical dose-finding studies with topical antimycotics.

## Publication Types:

- Clinical trial
- Randomized controlled trial

PMID: 7658304, UI: 95387223

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## Pharmacology of the allylamines.

Birnbaum JE

Sandoz Research Institute, East Hanover, NJ 07936.

The allylamines are a new class of antifungal drugs that inhibit ergosterol synthesis at the level of squalene epoxidase. These agents are highly selective for the fungal enzyme and have a minimal effect on mammalian cholesterol synthesis. Naftifine, the original member of the allylamine series, possesses only topical activity, whereas the naftifine analog terbinafine is active both topically and orally. In vitro, terbinafine is exceptionally active against dermatophytes, molds, and dimorphic fungi in which it exerts a fungicidal action. This in vitro profile is reflected by the clinical effectiveness of this allylamine in the treatment of dermatophyte infections. When given orally, terbinafine is well absorbed and rapidly and extensively distributed to the skin and sebum in concentrations that exceed the minimum inhibitory concentrations of these organisms by several orders of magnitude.

## Publication Types:

- Review
- Review, tutorial

PMID: 2229523, UI: 91036217

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Combining hydrocortisone with an antifungal on the skin.

PMID: 4042874, UI: 86004155

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1: *Ann Dermatol Venereol* 1993;120(1):21-31

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[New antifungal agents in the treatment of superficial dermatomycoses].

[Article in French]

Degreef H

Universite Catholique de Leuven, Hopital Universitaire, Departement de Dermatologie, Belgique.

New antifungals for topical and systemic treatment of superficial mycotic infections of the skin and nails have been developed in the last decade. Terconazole is a potent drug in treating topically vaginal candidiasis. Amorolfine belongs to the chemical class of morpholine derivatives and is topically active against a wide range of fungal infections. Also naftifine and terbinafine, two new allylamines, can be used in local therapy of superficial mycotic infections of the skin. Itraconazole and fluconazole are both new triazoles for systemic use. Itraconazole has a broader spectrum and a higher safety profile than ketoconazole, caused by a greater specificity for the fungal cytochrome P 450 14-alpha-demethylase. The pharmacokinetic properties result in shorter treatments, even in onychomycosis. The mode of action of fluconazole is the same as for the azoles. This drug was being studied particularly in systemic mycoses and mucosal candidiasis. The activity of orally terbinafine is directed mainly against dermatophytes. This drug offers new therapeutic possibilities in the treatment of onychomycosis, caused by dermatophytes.

## Publication Types:

- Review
- Review, tutorial

PMID: 8393313, UI: 93332354



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## Topical antifungal agents: an update.

Diehl KB

Medical Center of Delaware, Wilmington, USA.

So many topical antifungal agents have been introduced that it has become very difficult to select the proper agent for a given infection. Nonspecific agents have been available for many years, and they are still effective in many situations. These agents include Whitfield's ointment, Castellani paint, gentian violet, potassium permanganate, undecylenic acid and selenium sulfide. Specific antifungal agents include, among others, the polyenes (nystatin, amphotericin B), the imidazoles (metronidazole, clotrimazole) and the allylamines (terbinafine, naftifine). Although the choice of an antifungal agent should be based on an accurate diagnosis, many clinicians believe that topical miconazole is a relatively effective agent for the treatment of most mycotic infections. Terbinafine and other newer drugs have primary fungicidal effects. Compared with older antifungal agents, these newer drugs can be used in lower concentrations and shorter therapeutic courses. Studies are needed to evaluate the clinical efficacies and cost advantages of both newer and traditional agents.

PMID: 8857790, UI: 97010757

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1: *Antimicrob Agents Chemother* 1996 Feb;40  
(2):443-7

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## Characterization of squalene epoxidase activity from the dermatophyte *Trichophyton rubrum* and its inhibition by terbinafine and other antimycotic agents.

Favre B, Ryder NS

Department of General Dermatology, SANDOZ Research Institute, Vienna, Austria.

Squalene epoxidase (SE) is the primary target of the allylamine antimycotic agents terbinafine and naftifine and also of the thiocarbamates. Although all of these drugs are employed primarily in dermatological therapy, SE from dermatophyte fungi has not been previously investigated. We report here the biochemical characterization of SE activity from *Trichophyton rubrum* and the effects of terbinafine and other inhibitors. Microsomal SE activity from *T. rubrum* was not dependent on soluble cytoplasmic factors but had an absolute requirement for NADPH or NADH and was stimulated by flavin adenine dinucleotide. Kinetic analyses revealed that under optimal conditions the  $K_m$  for squalene was 13  $\mu\text{M}$  and its  $V_{\text{max}}$  was 0.71 nmol/h/mg of protein. Terbinafine was the most potent inhibitor tested, with a 50% inhibitory concentration ( $IC_{50}$ ) of 15.8 nM. This inhibition was noncompetitive with regard to the substrate squalene. A structure-activity relationship study with some analogs of terbinafine indicated that the tertiary amino structure of terbinafine was crucial for its high potency, as well as the tert-alkyl side chain. Naftifine had a lower potency ( $IC_{50}$ , 114.6 nM) than terbinafine. Inhibition was also demonstrated by the thiocarbamates tolciclate ( $IC_{50}$ , 28.0 nM) and tolnaftate ( $IC_{50}$ , 51.5 nM). Interestingly, the morpholine amorolfine also displayed a weak but significant effect ( $IC_{50}$ , 30  $\mu\text{M}$ ). *T. rubrum* SE was only slightly more sensitive (approximately twofold) to terbinafine inhibition than was the *Candida albicans* enzyme. Therefore, this difference cannot fully explain the much higher susceptibility ( $>$  or  $=$  100-fold) of dermatophytes than of yeasts to this drug. The sensitivity to terbinafine of ergosterol biosynthesis in whole cells of *T. rubrum* ( $IC_{50}$ , 1.5 nM) is 10-fold higher than that of SE activity, suggesting that the drug accumulates in the fungus.



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[Ketoconazole. 3 years' experience with a new orally active broadspectrum antimycotic].

[Article in German]

Haneke E

~~Ketoconazole~~ is an orally high effective broad-spectrum antimycotic of the imidazole series. It is very well tolerated and stands out by its long-lasting therapeutic serum levels, lack of development of resistant fungi, simple administration and low toxicity. Own experience has shown its high efficacy in pityriasis versicolor, mycoses due to dermatophytes, ~~skin and mucous~~ membrane candidoses and chronic mucocutaneous candidosis syndromes. Its effect in systemic mycoses is promising. Consistent follow-up of laboratory data did not suggest any changes due to ketoconazole even after more than one year of treatment.

PMID: 6291267, UI: 83043532

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1: *Drugs* 1996 Apr;51(4):585-620

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Published erratum appears in *Drugs* 1996 Aug;52(2):253

**Itraconazole. A reappraisal of its pharmacological properties and therapeutic use in the management of superficial fungal infections.**

Haria M, Bryson HM, Goa KL

Adis International Limited, Auckland, New Zealand.

Itraconazole is an orally administered triazole antifungal agent. Its spectrum of activity includes dermatophyte, dimorphic and dematiaceous fungi, yeasts, and some moulds. In clinical trials, mycological cure was attained in approximately 70 to 80,  $\geq 70$  and  $\geq 80\%$  of patients with, respectively, fingernail and toenail onychomycosis (200 mg/day for 3 months), dermatophytosis (100 mg/day for 2 to 4 weeks) and vaginal candidiasis (400 mg/day for 1 day or 200 mg/day for 3 days). Approximately 20 to 30% of patients with onychomycosis may relapse after completion of therapy; relapse rate data are limited for the other indications. Recently developed intermittent regimens of itraconazole (400 mg/day for 1 week per month for 3 to 4 months) appear to have similar efficacy to standard regimens in the treatment of onychomycosis. Shorter, higher dosage itraconazole treatment regimens (200 or 400 mg/day for 1 week) are also beneficial in dermatomycoses. Discrepancies and limitations of study design hamper conclusions about efficacy relative to other antifungal drugs. Newer intermittent and short course higher dosage itraconazole regimens have also not been evaluated in comparative studies. Available studies show that the efficacy of itraconazole appears to be greater than that of griseofulvin, but similar to or lower than that of terbinafine in patients with dermatophyte onychomycosis or cutaneous fungal infections. Moreover, the efficacy of itraconazole may be similar to or lower than that of fluconazole in the treatment of cutaneous mycoses. Comparative data from patients with acute vaginal candidiasis suggest that itraconazole is at least as effective as intravaginal clotrimazole and oral fluconazole, and superior to intravaginal econazole. These results require confirmation. Prescription-event monitoring data indicate that itraconazole is generally well tolerated. Gastrointestinal disturbances, dizziness and headache occur most commonly; liver toxicity has been rarely described. Its usefulness in some clinical situations may be

limited because of its ability to interact with various therapeutic agents. In conclusion, itraconazole along with other established agents should be considered a first-line treatment for patients with extensive or recalcitrant cutaneous fungal infections, mixed dermatophyte and *Candida* onychomycosis or vaginal candidiasis. It is currently considered a second-line drug for dermatophyte onychomycosis; the use of newer intermittent itraconazole treatment regimens may, however, extend its role in the management of this condition. Although itraconazole offers greater benefit than conventional therapies (griseofulvin and ketoconazole) in terms of efficacy and tolerability, wider clinical experience is required to determine its merits relative to the newer agents, terbinafine and fluconazole.

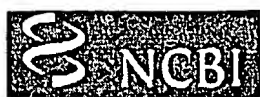
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PMID: 8706596, UI: 96261478



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## Fungal allergens.

Horner WE, Helbling A, Salvaggio JE, Lehrer SB

Department of Medicine, Tulane University Medical Center, New Orleans, Louisiana 70112, USA.

Airborne fungal spores occur widely and often in far greater concentrations than pollen grains. Immunoglobulin E-specific antigens (allergens) on airborne fungal spores induce type I hypersensitivity (allergic) respiratory reactions in sensitized atopic subjects, causing rhinitis and/or asthma. The prevalence of respiratory allergy to fungi is imprecisely known but is estimated at 20 to 30% of atopic (allergy-predisposed) individuals or up to 6% of the general population. Diagnosis and immunotherapy of allergy to fungi require well-characterized or standardized extracts that contain the relevant allergen(s) of the appropriate fungus. Production of standardized extracts is difficult since fungal extracts are complex mixtures and a variety of fungi are allergenic. Thus, the currently available extracts are largely nonstandardized, even uncharacterized, crude extracts. Recent significant progress in isolating and characterizing relevant fungal allergens is summarized in the present review. Particularly, some allergens from the genera *Alternaria*, *Aspergillus*, and *Cladosporium* are now thoroughly characterized, and allergens from several other genera, including some basidiomycetes, have also been purified. The availability of these extracts will facilitate definitive studies of fungal allergy prevalence and immunotherapy efficacy as well as enhance both the diagnosis and therapy of fungal allergy.

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PMID: 7621398, UI: 95346867

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## Nasal absorption of testosterone in rats.

Hussain AA, Kimura R, Huang CH

Testosterone levels in the blood were determined in rats following nasal, intravenous, and intraduodenal administration of 25-micrograms and 50-micrograms doses. The results indicated that the drug levels after nasal and intravenous administration were similar, whereas intraduodenal administration resulted in considerably lower levels. The bioavailability of the nasally administered drug was calculated to be 99% and 90% at the 25-micrograms and 50-micrograms doses, respectively. The intraduodenal bioavailability was only 1% at the dose studied.

PMID: 6491955, UI: 85033273

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1: *Dermatologica* 1983;166 Suppl 1:1-7

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Tioconazole, a new imidazole-antifungal agent for the treatment of dermatomycoses. Antifungal and pharmacologic properties.

Marriott MS, Baird JR, Brammer KW, Faulkner JK, Halliwell G, Jevons S, Tarbit MH

Tioconazole is a new imidazole antifungal agent with broad-spectrum activity. Its in vitro activity against common dermal pathogens is generally better than miconazole by a factor of 2-8. This activity is paralleled by good topical efficacy in a guinea pig dermatomycosis model. Pharmacokinetic studies in animals have demonstrated minimal systemic exposure following dermal application. Acute general pharmacology studies have shown that the compound is well tolerated in animals and unlikely to produce side-effects in man.

PMID: 6884559, UI: 83288013

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## Itraconazole: pharmacokinetics and indications.

Negroni R, Arechavala AI

Facultad de Medicina, Universidad de Buenos Aires, Hospital de Enfermedades Infecciosas Francisco J. Muniz, Argentina.

Itraconazole is a highly lipophilic triazolic compound, scarcely soluble in acidified polyethylene glycol, and soluble in hydroxypropyl-beta-cyclodextrin. It possesses an excellent digestive adsorption and its peak plasma level after oral administration of 100 mg is 0.16 microgram/ml at 3 or 4 h after drug intake. Half-life of itraconazole ranges between 17 to 21 h and 99.8% binds to plasmatic proteins, especially albumin. Metabolization is mainly done in the liver where inactive metabolites are formed with the exception of hydroxy-itraconazole, which exhibits a discrete antifungal activity. Stabilization of blood levels with repeated drug administration is reached at day 14, showing an increase both in plasma concentrations and in its half-life. Tissue levels of itraconazole are 3- to 20-fold higher than plasmatic concentrations, whereas only negligible concentrations are in CSF and urine. In the skin and particularly nails, itraconazole persists for a long time after discontinuation of therapy. Its mechanism of action is similar to other azolic compounds, inhibiting the alpha-14-demethylase of lanosterol which interferes with the synthesis of ergosterol. This drug behaves as a wide spectrum antifungal agent, acting against most pathogenic fungi with the exception of the Zygomycetes. Daily doses vary, according to indications, from 100 to 400 mg. The efficacy and results obtained in dermatomycosis, candidiasis, paracoccidioidomycosis, keratomycosis, sporotrichosis, chromoblastomycosis, coccidioidomycosis, blastomycosis, cryptococcosis, phaeohyphomycosis and maduromycotic mycetomas are detailed.

## Publication Types:

- Review
- Review, tutorial

PMID: 8118163, UI: 94162844



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[Penicillinosis of the paranasal sinuses].

[Article in German]

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A 29-year old female patient suffering from severe pain in her right eye, headache, ophthalmoplegia and ptosis of the right eye, total roentgenological opacity of the right maxillary sinus and ethmoidal cells, as well as signs of bone destruction in the orbital floor, was operated on under the suspicion of a tumour. Histological and bacteriological examinations as well as fungus cultures indicated, however, that the patient was suffering from a chronic infection caused by *Penicillium notatum*. Surgical treatment and postoperative intravenous administration of amphotericin B resulted in complete recovery of the patient.

PMID: 3531745, UI: 87013723

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[1% bifonazole lotion in the therapy of otomycosis].

[Article in Italian]

Piantoni S, Name S, Bottin R, Solazzo A, Bianchi W

Twenty-five patients suffering from otomycosis were treated once daily with bifonazole lotion 1% for a period of 4-15 days (means  $\pm$  DS 9.5  $\pm$  2.6 days). Two days before the end of the treatment complete resolution of the clinical picture in 23/23 patients was observed. Direct mycological and cultural examinations undertaken during the same control visit showed complete eradication of the responsible fungi in all 23 patients. Two-four weeks after the end of therapy a further control visit was carried out, during which 2/21 cases with clinical and mycological relapses were seen; both patients had chronic otitis. Tolerability of bifonazole was satisfactory in all cases but one, who interrupted treatment because of pain and local hyperemia where the lotion had been applied. In some patients suffering from chronic otitis application of the lotion caused slight and short-lasting pain and burning of the ear.

PMID: 2529076, UI: 90004141

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[Antimycotic therapy in clinical practice].

[Article in German]

Schaffner A

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Departement fur Innere Medizin, Universitatsspital Zurich.

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Mycoses commonly encountered in outpatients in Europe are usually limited to body surfaces and are no threat to the patient. Topical or systemic therapy with modern antimycotics is usually effective. Improved pharmacokinetic properties of newer azoles have shortened and simplified treatment of the mucosal forms of candidiasis for which a single dose of fluconazole (150 or 200 mg) or a short course with two doses of itraconazole (2 x 100 mg) are recommended. For patients with an uncorrectable predisposition to thrush, guidelines are provided for prophylaxis or self-initiated therapy. Whenever possible dermatophytoses should be treated topically to avoid long-term exposure to the new keratinotropic azoles and allylamines, for which insufficient long-term toxicological data are at present available. Ketoconazole should be avoided for these indications because of its potentially serious hepatotoxicity. For many indications requiring prolonged treatment, griseofulvin remains the favoured systemic drug due to its extensive safety record.

PMID: 1925472, UI: 92022441

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[Bifonazole for the topical treatment of surface mycoses--progress]!

[Article in German]

Schubert E, Binder D, Frank H

69 patients with superficial mycosis were treated with 1% Bifonazol cream once a day. 48 of them who suffered from tinea pedis interdigitalis received Bifonazol for 3 weeks, the remaining 21 patients who had superficial candidiasis applied it over a period of 4 weeks. The local tolerance of the cream has been very good. Control examinations 3 and 14 days after treatment proved 59 (89%) of all patients to be cured, i.e. 40 of those who had suffered from tinea pedis and 19 of the group with candidiasis.

PMID: 6528693, UI: 85144464

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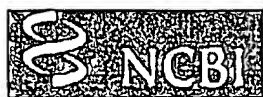
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1: *Clin Exp Allergy* 1996 Apr;26(4):444-51

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Allergenic components in three different species of *Penicillium*:  
crossreactivity among major allergens.

Shen HD, Lin WL, Tsai JJ, Liaw SF, Han SH

Department of Medical Research, Veterans General Hospital-Taipei, Taiwan,  
Republic of China.

**BACKGROUND:** *Penicillium* species have been considered as important causative agents of extrinsic bronchial asthma. However, little is known about the allergens of these ubiquitous airborne fungal species.

**OBJECTIVE:** This study compares the allergenic profiles and allergenic crossreactivity among allergens of three prevalent airborne *Penicillium* species. **METHODS:** IgE-binding *Penicillium* components were identified by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE)-immunoblotting using sera from 67 asthmatic patients. The presence of allergenic crossreactivity was analysed by immunoblot inhibition.

**RESULTS:** Among the 67 serum samples tested, 15, 14 and 11 samples showed IgE reactivity to components of *P. citrinum*, *P. notatum* and *P. brevicompactum*, respectively. All 15 *P. citrinum*-positive serum samples showed IgE-binding to a 33 kDa extract component of this species. Thirteen (93%) of the 14 *P. notatum*-positive serum samples and 10 (91%) of the 11 *P. brevicompactum*-positive sera also showed IgE reactivity to components with a molecular weight of about 33 kDa in individual *Penicillium* species. All of the 10 *P. brevicompactum* 33 kDa component-positive serum samples showed IgE reactivity to the 33 kDa components of the other two *Penicillium* species tested. Dose-dependent inhibition of IgE-binding to these major allergens was observed when the positive serum sample was absorbed with different amounts of individual allergenic extract as well as with different amounts of extracts prepared from the other two *Penicillium* species. **CONCLUSION:** Although different allergenic profiles were observed in the three different *Penicillium* species tested, results showed that there was an IgE crossreactivity among the 33 kDa group major allergens of *P. citrinum*, *P. notatum* and *P. brevicompactum*.

PMID: 8732242, UI: 96298843

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1: *Curr Med Res Opin* 1987;10(6):390-6

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## Bifonazole in the treatment of fungal skin infections in the tropics: a clinical and mycological study.

Soyinka F

A study was carried out in 40 patients with various superficial fungal diseases, confirmed by culture or microscopic examination, to assess the therapeutic efficacy and local tolerability of 1% bifonazole cream. Patients with more than one clinical diagnosis at the time of entry were treated according to the number of conditions present. The cream was applied once daily to the affected areas and treatment duration varied according to persistence or resolution of the clinical signs and symptoms in the individual patient. The results were evaluated by clinical and mycological examination 3 and 14 days after the end of treatment. A cure rate of 100% was achieved in cases of pityriasis versicolor, tinea corporis and candidiasis, and 90% in patients with tinea pedis. Clinical signs and symptoms disappeared completely in all but a few patients. No side-reactions were observed in any patient, and patch tests carried out in selected patients with known allergy and those with normal skin showed no evidence of any allergic or photosensitivity reaction to bifonazole.

PMID: 3568751, UI: 87189163

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1: *Arzneimittelforschung* 1983;33(5):750-4

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## Tolerability and efficacy of bifonazole in dermatomycoses.

Stettendorf S

1-[(4-Biphenyl)-phenylmethyl]-1-H-imidazole (bifonazole, Bay h 4502, Mycospor) is a broad-spectrum antifungal agent for the topical treatment of dermatomycoses. In addition to tolerability studies, a report is given on the results of 43 clinical studies of efficacy and tolerability involving 1129 patients in various countries. These were placebo-controlled double-blind studies, randomised comparative studies with reference preparations and open studies. They were carried out with bifonazole cream 1%, solution 1%, gel 1% and powder 1%. 58.6% of the patients tested suffered from dermatophytoses, 21.9% cutaneous candidoses, 14.3% from pityriasis versicolor and 5% from other skin infections. The therapeutic efficacy of bifonazole, assessed according to mycological and clinical findings proved good for the indications studied and administered once daily for a treatment period of 2 or 3 weeks. Tolerability - local and systemic - was good. There was no evidence of substance-related side effects.

## Publication Types:

- Clinical trial
- Randomized controlled trial

PMID: 6683554, UI: 83256820

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1: *Clin Exp Allergy* 1996 Jul;26(7):794-8

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Sensitization to *Alternaria* and *Cladosporium* by the age of 4 years.

Tariq SM, Matthews SM, Stevens M, Hakim EA

Asthma &amp; Allergy Research Centre, St Mary's Hospital, Newport, Isle of Wight, UK.

Of 1218 children born on the Isle of Wight in 1989/90, and followed for atopy at age 4 years, 981 were skin-prick tested with a battery of allergens. Of these 61 (6%) reacted positively to *Alternaria alternata* and *Cladosporium herbarum* (47 to *Alternaria*, 21 to *Cladosporium* and seven to both). Twenty-four (39%) were asymptomatic (latent atopy) of which 12 had a single positive reaction either to *Alternaria* or *Cladosporium*. Asthma was the most common disease in children sensitized to moulds. *Alternaria* sensitization correlated positively with clinical diagnosis of asthma ( $P < 0.01$ ), eczema ( $P < 0.001$ ) and rhinitis ( $P < 0.05$ ). Likewise, *Cladosporium* sensitivity correlated with a diagnoses of asthma, eczema and rhinitis (all  $P < 0.05$ ). Age of the house correlated with reported damp and lack of central heating (both  $P < 0.001$ ), but not with sensitization to moulds. An association between the presence of damp or age of the house and mould allergy was confounded by 21 children moving house in the first 4 years. Exposure to pets, passive tobacco smoking and season of birth had no bearing on mould sensitivity. At 4 years of age *Alternaria* and *Cladosporium* were the third most common causes of sensitization, i.e. after house dust mite and grass pollen.

PMID: 8842553, UI: 96440242

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1: *Pediatr Dermatol* 1997 Mar-Apr;14(2):146-8

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Itraconazole in the treatment of two young brothers with chronic mucocutaneous candidiasis.

Tosti A, Piraccini BM, Vincenzi C, Cameli N

Department of Dermatology, University of Bologna, Italy.

We report on two children affected by chronic mucocutaneous candidiasis involving the mouth and all the nails who were successfully treated with itraconazole at 200 mg/day for 2 months. This therapy produced a rapid cure of both candidal nail and mouth infections. The drug was very well tolerated, and routine laboratory monitoring during treatment did not reveal any abnormalities.

PMID: 9144703, UI: 97289918

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Mode of action of anti-Candida drugs: focus on terconazole and other ergosterol biosynthesis inhibitors.

Vanden Bossche H, Marichal P

Department of Comparative Biochemistry, Janssen Research Foundation, Beerse, Belgium.

A large proportion of the presently available antifungal agents are claimed to derive their activity from interaction with the biosynthesis of ergosterol, the key sterol in most pathogenic fungi. An important target for the allylamines, naftifine and terbinafine, is the squalene epoxidase. Interaction with the epoxidation step results in a decreased availability of ergosterol and an accumulation of squalene. Although the squalene epoxidase is clearly the primary target for this class of antifungals, it still remains an open question whether the fungistatic or fungicidal effects originate from a decrease in ergosterol or squalene accumulation. Indeed, preliminary evidence suggests that squalene does not change the physicochemical properties of membranes. Much more is known about the primary and secondary effects of the azole antifungals, such as miconazole, ketoconazole, terconazole, and itraconazole. Most of the imidazole and triazole derivatives are highly potent and selective inhibitors of the cytochrome P-450-dependent 14 alpha-demethylation of lanosterol (P-45014DM). Their potency and selectivity are determined by the nitrogen heterocycle and to a much greater extent by the hydrophobic N-1 substituent. The triazole antifungals, terconazole and itraconazole, combine a high affinity for Candida P-45014DM with an exceptionally low effect on mammalian cytochrome P-450.

PMID: 1951574, UI: 92059302

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